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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,449	02/05/2002	Gunter Muller	DEAV2001/0002	7390
5487	7590	01/25/2005	EXAMINER	
ROSS J. OEHLER AVENTIS PHARMACEUTICALS INC. ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			DUNSTON, JENNIFER ANN	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 01/25/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/067,449	Applicant(s) MULLER ET AL.	
	Examiner Jennifer Dunston	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 11-25 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3 and 27 is/are allowed.
- 6) ☒ Claim(s) 1,4-6, 8-10, 26 and 28 is/are rejected.
- 7) ☒ Claim(s) 2 and 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This action is in response to the Amendment, filed 9/29/2004, in which the specification was amended to include the date of deposit and the street address of the Budapest Treaty depository used for all deposited strains; claim 3 was amended; and claims 26-28 were added. Claims 1-10 and 26-28 are under consideration. Applicants' arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1, 4-6, 8-10, 26 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection has been slightly altered to include new claims 26 and 28.**

Claim 1 is drawn to yeast strains which can no longer grow on substrates with hexoses as the sole carbon source and whose ability to grow on a hexose can be restored when a Glut4 gene is expressed in the strain. Claim 8 recites a step of providing such a strain. The yeast strains must contain a mutation or combination of mutations that make the yeast strain unable to grow in the presence of hexoses as the sole carbon source in such a manner as to allow complementation by expression of a Glut4 transporter. Claims 26 and 28 are drawn to strains of the yeast

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Saccharomyces cerevisiae produced by the process claims 3 and 27, respectively. The *Saccharomyces cerevisiae* yeast strains are produced by random mutagenesis and thus contain undefined mutation(s) that allow the yeast strain, in which all hexose transporters have been eliminated, to grow on a substrate with a hexose as the only carbon source.

The rejected claim thus comprises a set of yeast strains with a genetic background that can be derived from any mutagenesis procedure resulting in any type of mutation, such as insertion, deletion, transition, transversion or gross rearrangement of the yeast genome. Mutations are not limited to known transporter genes. The mutations required for functional expression of a Glut4 transporter may include mutations that affect the trafficking of transmembrane proteins to the cell surface or that affect the respiratory capacity of the yeast, for example. Functionally, the yeast strain must not grow on hexoses as the sole carbon source; however, growth must be restored by the functional expression of a Glut4 transporter. Thus, the rejected claims encompass an enormous genus of yeast strains that must meet very specific functional limitations.

The instant specification describes a known yeast strain in which all of the transporters which are capable of taking up hexoses have been removed by deletion (Wieczorke et al., FEBS Lett. 464, 123-128, 1999). Wieczorke et al. teach that this strain is not capable of growing on a substrate with glucose as the sole carbon source. The instant specification teaches that this yeast strain requires further modification to allow for significant glucose transport into the yeast by a Glut4 transporter (e.g. page 4, lines 4-6; page 23, lines 10-29). Yeast strains expressing Glut4 from a plasmid vector carrying a Glut4 gene under the control of a yeast promoter are transformed into the yeast, and yeast cells containing mutation(s) are identified by growth on a

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substrate with glucose as the sole carbon source. There is no description in the specification as originally filed of the mutations that meet the claim limitations. For example, strains DSM 14038, DSM 14039 and DSM 14040 listed in table 1 contain unspecified mutation(s) that allow for complementation of the growth phenotype by a Glut4 transporter. It is not possible from reading the examples to envision what types of mutations have been introduced, how many mutations have been introduced in each yeast strain or which genes have incurred mutations.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claim with regard to structure and function, the examples are only representative of a few yeast strains within the broad genus of yeast strains embraced by the rejected claims that actually meet the functional limitations of the claims. The results described are not predictive of the mutation, or combination of mutations, required for the generation of a yeast strain that cannot grow on a hexose as a sole carbon source, where complementation of this phenotype can be achieved by expression of a Glut4 gene. It is impossible for one to extrapolate from the few uncharacterized yeast strains described herein those yeast strains that would necessarily meet the structural/ functional characteristics of the rejected claims.

Therefore, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those mutations or combination of mutations that 1) prevent the growth of a given strain of *Saccharomyces cerevisiae* on hexoses as a sole carbon source and 2) allow complementation of the growth phenotype by expression of a Glut4 gene under the control of a yeast promoter. Therefore, one of skill in the art would not have been able to envision a representative number of specific mutations or combination of mutations sufficient to describe the broad genus of yeast strains encompassed by the rejected claims. One

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of skill in the art would thus have reasonably concluded the applicant was not in possession of the claimed invention.

Response to Arguments Claim Rejections - 35 USC § 112 (written description)

Applicant's arguments filed 9/29/2004 have been fully considered but they are not persuasive. The response argues that (i) the instant claims are not to the entire genome-scope of *Saccharomyces cerevisiae* but define the claimed strain genus in both structural and functional terms, fully, (ii) Applicants have no duty under 35 U.S.C. 112, first paragraph, to provide an exhaustive teaching of different combinations of mutations capable of producing a *Saccharomyces cerevisiae* strain which cannot grow on hexoses as the only carbon source, and (iii) Applicants disclose that they have isolated and described nine such strains. This argument has been thoroughly reviewed but was not found to be persuasive because the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function (see MPEP 2163[R-2](I)(A)). The specification discloses nine strains that meet the functional limitations of the claims, however, the mutations in the strains have not been described in the specification. Therefore, there is no known structure that results in the functional expression of Glut4 in these nine strains. Without any known structure, one of skill in the art is unable to envision any additional members of the broad genus of yeast strains claimed. The specification does not provide any indication regarding as to whether a saturating mutagenesis screen was performed. The specification does not describe the number of different genes that can be mutated to result in

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the functional expression of Glut4 in a strain of the yeast *Saccharomyces cerevisiae* which can no longer grow on substrates with hexoses as the only carbon source. For example, each of the nine strains could have a mutation in a different gene in a different biochemical pathway.

Alternatively, all nine strains could have a mutation in the same gene, which would lead one of skill in the art to believe that the mutations that allow functional Glut4 expression are limited.

For one of skill in the art to make this determination, some structural information regarding the mutations in the identified strains would need to be described. Since the instant application does not provide this description, the nine strains that are disclosed in the instant specification do not provide sufficient written description for the claimed genus of *Saccharomyces cerevisiae* yeast strains which can no longer grow on substrates with hexoses as the sole carbon source and whose ability to grow on a hexose can be restored when a Glut4 gene is expressed in the strain.

Allowable Subject Matter

Claims 3 and 27 are allowed.

Claims 2 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jennifer Dunston
Examiner
Art Unit 1636

jad


TERRY MCKELVEY
PRIMARY EXAMINER